

Local Variation in Cutaneous and Subcutaneous Blood Flow Measured by CdTe(Cl) Minidetectors in Normal and Psoriatic Skin

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The accuracy of the ^{133}Xe washout method and the validity of newly developed cadmium telluride CdTe(Cl) minisemiconductor detectors were estimated by performing comparative, simultaneous measurements of both cutaneous (CBF) and subcutaneous (SBF) blood flow using 2 conventional scintillation sodium iodide NaI(Tl) and CdTe(Cl) detectors over the same radioactive depot in each of 10 individuals. The accuracy of the ^{133}Xe washout method was found to be 13–15% (C.V.) for the CBF measurements and 9–12% (C.V.) for the SBF measurements. The CdTe(Cl) detectors, which have a weight of 20 g and were attached directly over the radioactive depot, may replace stationary NaI(Tl) detectors placed 20 cm from the depot for measurements of both CBF and SBF. Two CdTe(Cl) detectors were used for estimations of the local variation in CBF and SBF within a distance of 5 cm in normal skin of 10 individuals. The C.V. was 7% for the CBF measurements and 18% for the SBF measurements. Measurements of CBF and SBF were performed in 6 psoriatic patients who, after

about 1 week of antipsoriatic treatment with beech tar, developed typical Woronoff rings. The local CBF differed significantly from the center of psoriatic plaques to the margin, in the Woronoff ring, and in nonlesional skin. In contrast, SBF was remarkably equal within the plaque and in the Woronoff ring. The color of the Woronoff ring cannot be ascribed to a local cutaneous vasoconstriction. Cutaneous blood flow in chronic stable, lesional psoriatic skin was significantly lower than previously published values for active lesional psoriatic skin, but significantly higher than CBF in normal individuals. Measurements of CBF in tetrahydrofurfuryl nicotinic acid (Trafuril)-treated skin showed higher values than measurements of CBF in the postischemic hyperemia period both in normal and in lesional psoriatic skin. Trafuril induced a significant increase of CBF in both lesional and nonlesional skin. The high CBF rates in lesional psoriatic skin are not due to a maximally, passively dilated vascular bed. *J Invest Dermatol* 86:109–114, 1986

During the last few years several reports have been published concerning significant abnormalities in the microvasculature and peripheral blood flow in psoriasis [1–14]. Undoubtedly, such factors play an essential role in the pathogenesis. By a plethysmographic technique, Thune [15] found evidence to suggest that the vascular dilatation is maximal. Ryan [1] has reviewed the literature on microcirculation in psoriasis and questioned whether cutaneous blood flow (CBF) was sufficient to meet the metabolic demand in lesional psoriatic skin. We have recently shown that CBF in lesional psoriatic skin was about 10 times higher than CBF in normal individuals under normal conditions [8,13] and that it might even be slightly higher than the estimated maximal CBF in normal individuals [16]. The high CBF in lesional psoriatic skin might, therefore, represent a maximal CBF. In this study we have examined whether the arterioles in psoriatics are capable of active dilation, i.e., increasing CBF and thus adjusting the blood flow to an increased metabolic demand, or whether the

high CBF in lesional psoriatic skin is a passive, maximally dilated vascular bed.

During successful antipsoriatic treatment the high CBF of lesional psoriatic skin decreases [10,13,17]. After about 1 week of antipsoriatic treatment a white ring just outside the lesion may appear [18–24]. The nature of this white ring—the Woronoff ring—is unknown. Its color might indicate that a vascular phenomenon analogous to the white dermographism or blanching reaction could be involved [25]. Measurements of local variations of CBF in patients with psoriasis would, therefore, be valuable.

The ^{133}Xe washout technique has previously been used for quantitative measurements of CBF and subcutaneous blood flow (SBF) in patients with psoriasis [8,11–14]. With the conventional scintillation sodium iodide [NaI(Tl)] detector-equipment it is difficult, however, to obtain simultaneous comparable measurements within a small area of skin. Recently, a miniature cadmium telluride CdTe(Cl) detector, which could be attached directly to the skin, has been developed and was found capable of measuring local SBF [26–28]. Theoretically, a small detector placed over a radioactive depot in a small area of skin might be used to measure the local CBF.

MATERIALS AND METHODS

Patients and Controls A total of 118 washout curves was obtained from 38 individuals. Age and sex distributions in each experimental series are shown in Tables I–IV. None of the subjects received any medication that might be suspected to interfere with peripheral blood flow. None of the patients in whom the effect of tetrahydrofurfuryl nicotinic acid (Trafuril, CIBA Geigy) was tested received salicylic acid, which is a known inhibitor of Trafuril [29]. For this reason local treatment with salicylic ointment, which theoretically might inhibit the effect of Trafuril, was

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Abbreviations:

- CBF: cutaneous blood flow
- CdTe(Cl): cadmium telluride
- LDV: laser Doppler velocimetry
- NaI(Tl): sodium iodide
- SBF: subcutaneous blood flow
- C.V.: coefficient of variation

Table I. Comparison of Simultaneously Measured Cutaneous and Subcutaneous Washout Rates from One Depot

Subject	Age	Sex	CdTe(CI)		NaI Vertical		NaI from Below	
			Cutis	Subcutis	Cutis	Subcutis	Cutis	Subcutis
1	66	F	5.41 (0.09)	0.72 (0.02)	6.75 (0.32)	0.73 (0.04)	8.41 (0.26)	0.73 (0.05)
2	19	F	9.73 (0.05)	0.34 (0.03)	13.00 (0.32)	0.34 (0.04)	11.05 (0.19)	0.27 (0.04)
3	48	M	9.34 (0.08)	0.53 (0.03)	9.07 (0.08)	0.40 (0.04)	9.09 (0.14)	0.40 (0.04)
4	50	F	11.34 (0.17)	0.47 (0.03)	8.57 (0.18)	0.55 (0.05)	7.81 (0.28)	0.41 (0.06)
5	20	F	10.15 (0.20)	0.33 (0.01)	13.06 (0.68)	0.37 (0.05)	12.93 (0.56)	0.30 (0.04)
6	39	F	12.86 (0.16)	0.26 (0.02)	10.57 (0.13)	0.28 (0.05)	12.87 (0.28)	0.24 (0.04)
7	69	M	11.67 (0.13)	0.43 (0.03)	11.70 (0.22)	0.46 (0.07)	12.05 (0.35)	0.38 (0.07)
8	59	F	10.14 (0.22)	0.31 (0.01)	11.39 (0.97)	0.28 (0.02)	9.81 (0.48)	0.33 (0.06)
9	17	F	12.08 (0.09)	0.59 (0.03)	14.12 (0.16)	0.58 (0.06)	11.86 (0.15)	0.40 (0.06)
10	56	M	8.59 (0.17)	0.25 (0.03)	7.55 (0.18)	0.22 (0.01)	11.29 (0.43)	0.21 (0.03)
Mean \pm SD	44 \pm 20		10.13 \pm 2.12	0.42 \pm 0.15	10.58 \pm 2.51	0.42 \pm 0.16	10.72 \pm 1.83	0.37 \pm 0.15

Three detectors were used: one CdTe(CI) minidetector attached to the skin over the radioactive depot, and 2 NaI(Tl) detectors placed 15 cm from the depot, one vertical to the field of vision of the CdTe(CI) detector and one placed beneath the depot. Washout rate ($\times 100 \cdot \text{min}^{-1}$) and 1 SD (in parentheses) are shown. For the statistical analysis see the text.

avoided. Smoking was not allowed for 3 h before the measurements.

Twenty patients suffering from minor dermatologic disorders (far from the measuring skin area), and all with clinically normal skin at the test site were selected for studies of the validity of the CdTe(CI) detectors (Tables I, II).

Six patients with an outburst of psoriasis and who developed typical Woronoff rings around the psoriatic lesions during treatment with beech tar were selected for studies of local variation in CBF and SBF (Table III).

Eight patients with untreated, chronic psoriasis were selected for studies of the capability to vasodilate (Table IV). One psoriatic patient and 3 normal individuals served as controls.

CdTe(CI) Detectors Semiconductor CdTe(CI) γ -sensitive detector units were used to follow the ^{133}Xe washout. The detector contains the detector crystal, a 1-mm cylindrical lead collimator, and the first stage of a charge-sensitive preamplifier (Memolog, Novo Diagnostic System). The detector measures 16 mm in diameter by 22 mm in height (weight 20 g) and is mounted on a 2-mm aluminum plate measuring 3.5×5.5 cm (weight 12 g). The detector plus the aluminum base plate exerts an external pressure against the skin surface of 1.2 mm Hg/cm^2 . The technical and geometric characteristics of this type of detector and the theoretical background for measurements of the SBF have recently been published [26–28].

NaI(Tl) Detectors Two standard NaI(Tl) scintillation detector crystals $3'' \times 3''$ with a wide-angle lead collimator (1 cm thick)

and an entrance aperture 7.5 cm in diameter with a depth of 7 cm were used for the comparative measurements.

Measurements of CBF and SBF The ^{133}Xe washout technique was used [30]. The method employed on psoriatic patients has recently been described [8,11–14], and the same methodologic procedure was followed. In the calculations of blood flow the following tissue-to-blood partition coefficients for ^{133}Xe (λ) were used: untreated, lesional psoriatic skin ($\lambda = 1.2 \text{ ml/g}$); nonlesional psoriatic skin; Woronoff ring and normal skin ($\lambda = 0.7 \text{ ml/g}$); lesional psoriatic skin treated with beech tar for 1–2 weeks ($\lambda = 1.0 \text{ ml/g}$); subcutaneous tissue ($\lambda = 5.0 \text{ ml/g}$) [8,12,13,30].

Comparison of the CdTe(CI) Detector and NaI(Tl) Detectors After atraumatic labeling of a 10-cm^2 skin area on the volar, proximal forearm the CdTe(CI) detector was gently attached to the skin over the radioactive depot. Two NaI(Tl) detectors were used for comparative measurements. One was placed 20 cm from the depot with its axis in the horizontal position and perpendicular to the vertical center axis of the CdTe(CI) detector. The other NaI(Tl) detector was placed in a vertical position 20 cm below the depot, thus looking in the opposite direction of the CdTe(CI) detector. The counting was performed simultaneously at all detector sites. Counts were printed out at 10-s intervals and recorded for at least 1.5 h. Calculations of the washout rate were performed from strictly simultaneous curve segments.

Theoretical Considerations Concerning Detectors Placed at Short Geometric Distance to the Radioactive Depot After

Table II. Local Variation in Simultaneously Measured Cutaneous and Subcutaneous Washout Rates in Normal Skin of 10 Individuals Using CdTe(CI) Detectors Attached to the Skin over the Radioactive Depots

Patient	Age	Sex	Cutis		Subcutis	
			Detector 1	Detector 2	Detector 1	Detector 2
1	27	M	14.00 (0.20)	14.03 (0.20)	0.91 (0.02)	1.19 (0.02)
2	37	F	6.76 (0.50)	8.83 (0.37)	0.48 (0.04)	0.35 (0.07)
3	55	M	8.33 (0.69)	8.75 (0.19)	0.33 (0.01)	0.26 (0.01)
4	40	F	9.03 (0.16)	12.22 (0.20)	0.60 (0.05)	0.53 (0.04)
5	36	M	9.85 (0.17)	9.56 (0.13)	0.66 (0.03)	0.45 (0.04)
6	55	F	7.82 (0.13)	8.05 (0.14)	0.50 (0.01)	0.36 (0.01)
7	16	F	31.30 (0.98)	31.03 (1.06)	0.89 (0.02)	0.89 (0.02)
8	52	F	10.48 (0.34)	9.93 (0.44)	0.40 (0.01)	0.49 (0.01)
9	63	M	10.67 (0.07)	10.90 (0.06)	0.71 (0.02)	0.56 (0.02)
10	46	M	9.20 (0.12)	9.82 (0.24)	0.44 (0.01)	0.42 (0.01)
Mean \pm SD	43 \pm 14		11.74 \pm 7.15 ^a	12.31 \pm 6.81 ^a	0.59 \pm 0.20 ^a	0.55 \pm 0.28 ^a

The detectors were placed at a distance of 5 cm. Washout rate ($\times 100 \cdot \text{min}^{-1}$) and 1 SD (in parentheses) are shown.

^ap is NS.

Table III. Local Variation in Cutaneous and Subcutaneous Blood Flow in Patients With Psoriasis Measured by CdTe(CI) Detectors After 7–10 Days of Treatment with Beech Tar

Patient	Age	Sex	Center LS		Margin LS		Woronoff Ring		NLS	
			Cutis	Subcutis	Cutis	Subcutis	Cutis	Subcutis	Cutis	Subcutis
1	24	M	39.1 (0.8)	3.80 (0.25)	9.1 (0.2)	4.10 (0.15)	9.7 (0.3)	4.05 (0.35)	4.2 (0.1)	2.85 (0.10)
2	27	F	18.7 (0.7)	1.15 (0.25)	19.3 (0.5)	1.15 (0.25)	16.0 (0.6)	1.95 (0.15)	7.4 (0.8)	1.15 (0.05)
3	36	F	33.0 (1.5)	2.55 (0.35)	32.0 (1.0)	3.10 (0.30)	22.6 (2.9)	2.95 (0.25)	5.5 (0.2)	4.80 (0.30)
4	68	F	33.4 (1.5)	5.35 (0.35)	32.2 (2.2)	3.85 (0.30)	11.5 (1.3)	2.85 (0.10)	9.1 (1.1)	2.10 (0.20)
5	28	M	35.0 (1.0)	4.25 (0.50)	23.7 (3.9)	4.80 (0.85)	15.7 (0.8)	4.35 (0.30)	7.3 (0.4)	2.65 (0.25)
6	72	M	21.3 (1.6)	4.35 (0.30)	20.8 (1.4)	4.15 (0.50)	12.5 (0.6)	5.45 (0.3)	6.8 (0.4)	3.30 (0.35)
Mean \pm SD	43 \pm 22		30.1 \pm 8.1 ^a	3.58 \pm 1.50 ^a	22.9 \pm 8.7 ^a	3.53 \pm 1.29 ^a	14.7 \pm 4.6 ^b	3.60 \pm 1.26 ^a	6.7 \pm 1.7 ^b	2.80 \pm 1.22 ^a

All patients had developed a typical Woronoff ring. All measurements were performed within the same skin area on the crus with a maximum radius of 4 cm. Blood flow in ml (100 g \cdot min)⁻¹. 1 SD is shown in parentheses. LS = lesional skin; NLS = nonlesional skin.

^a*p* is NS.

^b*p* < 0.05.

labeling, the ¹³³Xe might escape the cutaneous indicator depot by the following routes: (1) by blood; (2) by lymph; (3) by sweat; (4) by retrograde diffusion, i.e., either through the skin into the air, or by diffusion away from the blood—that leaves the depot—and into the surrounding tissue. The latter is physically a convection-diffusion process and is often designated as a relabeling process, and finally (5) by diffusion into the tissue surrounding the indicator depot, i.e., both parallel and vertical to the skin surface. Thus, the washout rate of ¹³³Xe is the integral of rates of disappearance from these 5 different routes. However, some of these factors are of minor practical importance or might be eliminated by the experimental setup. Removal of the ¹³³Xe by the lymph is quite insignificant since the local lymph flow is very low compared with the blood flow. During steady-state and thermostable conditions the loss of indicator by sweat is very small. Retrograde diffusion through the skin might be prevented using a Mylar membrane placed on the skin surface, although this route of indicator removal is only on the order of 1–2% of the total removal rate [30]. The relabeling process and the diffusion process might be eliminated by placing a wide-angle detector at a great distance from the radioactive field (“great” means relative to the possible absolute diffusion distance, i.e., 15–20 cm relative to a few mm). A detector placed at this distance should only measure the disappearance of indicator out of the field of view. The measured disappearance rate is therefore proportional to the blood flow rate. However, if the detector is placed close to the radioactive depot, the diffusion might significantly contribute to the total elimination rate. This point was recently demonstrated in a series of experiments where the washout rate constants were almost 1.5 times higher using CdTe(CI) detectors (attached to the skin over s.c. injected small ¹³³Xe depots) than the washout rate constants obtained simultaneously by NaI(Tl) detectors placed 15 cm from the radioactive depots [26]. Since ¹³³Xe is freely diffusible in tissue, diffusion processes take place in the periphery of the

depot due to the indicator concentration gradient. A way to overcome the influence of the local diffusion parallel to the skin surface might be to place a CdTe(CI) detector at the center of a uniformly labeled depot area several times larger than the field of view of the detector. In this way only diffusion away from the detector (i.e., deeper into the tissue) should—due to a decreased counting efficiency—be a source of overestimation of the true local elimination by blood flow. Since the diffusion of the indicator away from the detector still occurs within the field of view of the detector it might be of minor importance and probably beyond the limits of measuring accuracy. Simultaneous measurements of the washout rates, using NaI(Tl) detectors placed both horizontally and vertically opposed to the field of view of a CdTe(CI) detector, should reveal the uncertainty in the NaI(Tl) detector system and the validity of the CdTe(CI) detector.

Experimental Procedure

Comparison of CBF or SBF Measurements Using CdTe(CI) Detectors Within a Small Area of Clinically Normal Skin: In order to compare measurements of CBF or SBF in patients with diseased skin it is essential to know both the accuracy of the method and the normal range of variation in the blood flow within a small area of skin. The local variation in CBF and SBF was, therefore, studied in 10 subjects. Two CdTe(CI) detectors were placed at a distance of 5 cm from each other on the anterior middle part of the thigh during the measurements.

Measurements of Variation in CBF and SBF in Small Areas of Lesional and Nonlesional Psoriatic Skin During Treatment (“CBF in the Woronoff Ring”): Four CdTe(CI) detectors, each equipped with a collimator to observe a skin area of 2.5 \times 15 mm, were placed as follows: (1) in the center of a psoriatic plaque; (2) in the margin of the psoriatic plaque; (3) in the middle of the Woronoff ring; and (4) in nonlesional skin. All detectors were placed within a circle with a maximal radius of 4 cm.

Measurements of CBF and SBF in Lesional and Nonlesional Psoriatic Skin During Vasodilatation Achieved by Epicutaneous Application of Tretinoin: Pilot studies in Tretinoin-treated skin areas of 10 patients were performed by laser Doppler velocimetry (LDV) equipment, which gives a rough qualitative estimation of changes in the CBF in skin at high perfusion rates [13]. These experiments showed that Tretinoin ointment induces a rapid (i.e., less than 5 min) increase in CBF, and that a plateau of constant and high CBF was reached within 10 min and lasted at least 1.5 h in both lesional and nonlesional psoriatic skin.

The pharmacologic action of Tretinoin on cutaneous and subcutaneous vasculature is unknown. Previously, it was reported that Tretinoin might cause a moderate, dermal edema [29], which should influence the tissue-to-blood partition coefficient (λ) for ¹³³Xe and thus cause an overestimation of the CBF calculated in areas treated with Tretinoin. In order to estimate this edema quan-

Table IV. Mean Cutaneous and Subcutaneous Blood Flow of 8 Patients with Chronic, Stable Psoriasis [5 Men and 3 Women, Aged 53 \pm 15 yr (SD)] Before and After Epicutaneous Application of Tretinoin

	NLS	NLS + Tretinoin	LS	LS + Tretinoin
CBF ml (100 g \cdot min ⁻¹)	6.8 ^a (1.7)	23.2 ^a (7.3)	33.6 ^b (10.9)	51.4 ^b (15.5)
SBF ml (100 g \cdot min ⁻¹)	3.0 ^c (1.3)	3.7 ^c (1.9)	4.2 ^c (2.3)	7.6 ^c (6.6)

Measurements were performed with the CdTe(CI) detectors. One SD is shown in parentheses. NLS = nonlesional skin; LS = lesional skin.

^a*p* < 0.01.

^b*p* < 0.05.

^c*p* is NS.

tatively the thickness of skin was measured in 20 areas treated with Trafuril. Skin thickness was measured by means of a 15-MHz ultrasound B-mode probe, assuming that any increase in skin thickness due to the Trafuril treatment could be ascribed to a local edema. Calculations of the λ value were performed from previously published values of the skin content of lipid, water, and protein content in psoriatic and normal skin, respectively [8,30].

Control measurements of CBF and SBF [CdTe(Cl)] before and after ischemia for 5, 10, and 20 min in Trafuril-treated and untreated skin were performed in 4 individuals in order to estimate maximal CBF. Ischemia was induced by a manometer cuff inflated to 220 mm Hg. The measurements were compared with simultaneous measurements in Trafuril-treated and untreated skin areas proximal to the manometer cuff.

Statistical Analysis and Presentation of the Results: Unless otherwise stated, the Wilcoxon rank sum test for paired and unpaired samples was used for statistical analysis of the data. The p values less than 0.05 were considered to be significant. The least-squares method was used for regression analysis. The washout rate constant was expressed as $100 \cdot \text{min}^{-1}$ and the blood flow rate as $\text{ml} \cdot (100 \text{ g} \cdot \text{min})^{-1}$. C.V. denotes the coefficient of variation, calculated as previously described [26–28].

RESULTS

NaI(Tl) vs NaI(Tl) Detector Comparison The results are shown in Table I.

CBF: There was no statistically significant difference between the washout rates obtained with the 2 detectors. C.V. was 13%.

SBF: The calculated mean SBF was 12% lower using the NaI(Tl) detector placed below the depot compared with the measurements with the NaI(Tl) detector placed over the depot. The difference was statistically significant, $p < 0.05$. C.V. was 12%.

CdTe(Cl) vs NaI(Tl) Detector Comparison The results are shown in Table I.

CBF: There was no statistically significant difference between the washout rates obtained by the CdTe(Cl) detector and the horizontal or the vertical NaI(Tl) detector. C.V. was 15%.

SBF: There was no statistically significant difference between measurements obtained by the CdTe(Cl) and the NaI(Tl) detector placed horizontally. NaI(Tl) detector measurements (from below the depot) gave statistically, significantly lower values (mean 12%) than the CdTe(Cl) detector measurements. C.V. was 9%.

Two-way analysis of variance showed that the NaI(Tl) detector placed below the depot gave statistically, significantly lower SBF values than the 2 other detectors.

There was no statistically significant difference between the above mentioned C.V. values (F-test)

Local Variation in CBF and SBF Within a Distance of 5 cm: CdTe(Cl) Detector Measurements in Normal Skin Areas The results are summarized in Table II.

The intraindividual C.V. was 7% for the CBF measurements and 18% for the SBF measurements. The interindividual C.V. was 58 and 43% for CBF and SBF measurements, respectively. The difference between the intra- and interindividual C.V. was statistically significant, $p < 0.001$.

Local Small Area Variation of CBF and SBF in Lesional and Nonlesional Psoriatic Skin The results obtained by the CdTe(Cl) detectors are shown in Table III.

Effects of Trafuril on CBF and SBF in Nonlesional and Lesional Psoriatic Skin The results are summarized in Table IV.

Cutaneous blood flow in nonlesional skin was significantly lower than previously published CBF values in nonlesional psoriatic

skin [$9.5 \text{ ml} \cdot (100 \text{ g} \cdot \text{min})^{-1}$] [13], $p < 0.05$, but significantly higher than CBF in normal subjects [$4.7 \text{ ml} \cdot (100 \text{ g} \cdot \text{min})^{-1}$] [13], $p < 0.05$.

Control Studies

Skin Thickness Measurements in Trafuril-Treated and Untreated Skin: The mean skin thickness increased from $1.14 \pm 0.12 \text{ mm}$ (SD) in untreated control skin to $1.42 \pm 0.18 \text{ mm}$ (SD) in Trafuril-treated skin. The difference was statistically significant.

Effect of Ischemia and Trafuril on CBF: Cutaneous blood flow measurements during the postischemic period increased by increasing length of the ischemic period. The maximal CBF was, however, observed in the Trafuril-treated skin area. Measurements of CBF during the postischemic hyperemia period in the Trafuril-treated skin showed higher values than simultaneous measurements in adjacent nontreated skin areas. The highest measured CBF in the normal individuals was about $40 \text{ ml} \cdot (100 \text{ g} \cdot \text{min})^{-1}$.

DISCUSSION

The accuracy of CBF measurements using the ^{133}Xe washout method has not previously been published. Our results show that the methodologic accuracy of the ^{133}Xe washout technique is about 13–15% for the CBF measurements and about 9–12% for the SBF measurements. Recently, we [28] have reported a C.V. value for SBF measurements of the same magnitude, i.e., 9–11%. The statistically significant difference between the SBF values, measured simultaneously by the 2 NaI(Tl) detectors, is probably due to a combined effect of 2 phenomena [26]. First, there is an inhomogeneous attenuation and scatter of the low-energy γ -rays from the bones and tissue located in between the vertical NaI(Tl) detector and the subcutaneous ^{133}Xe depot (i.e., shadow effect). Second, the ^{133}Xe disappears very slowly from the subcutaneous adipose tissue. The results, therefore, show that ^{133}Xe measurements for SBF quantitations should not be performed with interposed bone-tissue between the detector and the radioactive depot.

A hypothetically higher washout rate due to diffusion deeper into the tissue does not seem to be of practical importance for the results. Cadmium telluride detectors may, therefore, substitute for the stationary NaI(Tl) detectors in measurements of both local CBF and SBF. The CdTe(Cl) detector has several clear-cut advantages over the stationary NaI(Tl) detector: it is portable, and measurements of CBF should, therefore, be possible during nonsteady-state conditions. Furthermore, simultaneous measurements might be performed at several sites of the body or in several small areas within an anatomically small area. Less radioactive doses might be used.

The results clearly show that the mean local variation of both CBF and SBF is minimal and of no practical significance within small skin areas. Comparative measurements of the local blood flows should therefore be possible—also in diseased skin.

The pale zone, which is often visible around psoriatic lesions, was described more than 100 years ago. The nature of this phenomenon has, however, been only sparsely investigated. In 1926 Woronoff [18] observed that psoriatic lesions, which developed a pale zone in the nonlesional, normal skin surrounding the psoriatic lesions, did not show signs of expansive growth. Woronoff observed that characteristic histologic features were found in these pale halos, and that the histologic demarcation of both lesional and nonlesional skin was well defined. Parakeratosis was not observed, the stratum corneum was broader and more compact than that in the adjacent, normal skin; the papillae were irregular; and the vessels were not dilated. Using capillary microscopy of untreated psoriatic lesions during a spontaneously healing process, Bettman [19] discovered that the capillaries in this pale zone were oriented horizontally, pointed toward the center of the plaque, and that these changes preceded the clinical manifestation of the Woronoff ring. Gougerot and Degot [20–22] described a ring that

was invisible in ordinary light, but visible with Wood's lamp. Microscopically, the vessels of these rings were dilated. Later Herrmann and Kanof [23] observed that i.v. injection of fluorescein occasionally produced a bright halo around the clinical lesions; and, in contrast to the observations by Woronoff [18] and Bettmann [19], these hyperfluorescent halos were detectable even in young lesions. When the lesions healed from the periphery inward, the halo zones broadened. When the healing occurred at the center of a lesion, this area became hyperfluorescent [23].

Penneys et al [24] injected prostaglandin E_2 i.d. 1 cm outside of a Woronoff ring. The injection produced redness in the Woronoff ring, whereas injection of saline did not. Biochemical analysis showed that the prostaglandin E_2 level was significantly reduced compared to values obtained from adjacent nonlesional skin or normal controls. The hypothesis was set forth that an inhibitor of prostaglandin synthesis diffuses outward from the psoriatic plaque during the healing process.

The result of the present study strongly indicates that the color of the Woronoff ring is not associated with the white dermographism or blanching reactions, since the CBF in nonlesional skin was significantly lower than the CBF in the Woronoff ring. It is, therefore, reasonable to assume that the color of the Woronoff ring is due to optical properties of the pseudoatrophic skin.

In this study vasodilation of the cutaneous vascular bed was achieved by epicutaneous application of Tretinoin. The effects of Tretinoin on the vasculature are unknown. Evidence of a direct and/or an indirect prostaglandin-like action of the tetrahydrofurfuryl nicotinate on the vessels has been reported [31-34].

The LDV measurements showed that the duration of the Tretinoin-induced, high perfusion rate was sufficient to allow for ^{133}Xe measurements. The increased skin thickness, which was quantified by the ultrasound measurements of skin thickness, showed that even if the entire increase in skin thickness was ascribed to an increase in water content, the influence on the tissue-to-blood partition coefficient (λ) would be only about 6-7%. Since an increased skin thickness after Tretinoin treatment might also be caused by an increase in the blood volume of the skin, the real change in the λ value should be less than 6-7%. Therefore, calculations of CBF were performed using the same λ value for both Tretinoin-treated and untreated skin [8].

The control measurements of CBF during postischemic hyperemia periods showed that considerably higher CBF rates were measured in the Tretinoin-treated skin compared to simultaneous measurements in untreated skin areas. Measurements of postischemic CBF, therefore, do not represent maximal CBF values. The results, however, showed that Tretinoin also occasionally caused dilatation of the subcutaneous vascular bed. The CBF values in the Tretinoin-treated skin do not represent maximal CBF values. This is strongly supported by the observation of higher CBF values in Tretinoin-treated skin areas during postischemic hyperemia periods in the control studies, although these values did not reach the values of the estimated maximal CBF in normal individuals, i.e., $40-50 \text{ ml} \cdot (100 \text{ g} \cdot \text{min})^{-1}$ [16].

The obtained mean CBF values of untreated, lesional psoriatic skin [$33.6 \text{ ml} \cdot (100 \text{ g} \cdot \text{min})^{-1}$, Table IV] were statistically significantly lower than we have previously published (63.6 [8] and $62.5 \text{ ml} \cdot (100 \text{ g} \cdot \text{min})^{-1}$ [13]). This is presumably due to differences in the types of psoriasis. In the present study the vasodilating capability was studied in a group of patients with chronic, stable psoriasis, whereas the previously published values were measured in patients with an outburst of psoriasis, i.e., active psoriasis. Also, the CBF in nonlesional skin of the patients in this study was statistically significantly lower than previously published [13]. Thus, as has been concluded by Ryan, it is essential to distinguish between active and chronic, stable psoriasis [1]. In a review on microcirculation in psoriasis, Ryan [1] questioned whether the CBF was sufficient to meet the metabolic demand in lesional psoriatic skin. The present results clearly show that the vasculature of chronic, stable psoriatic skin is not maximally dilated, but capable of further dilation, thus causing an increase in CBF

by a factor of about 1.5. Accordingly, previous results have shown that the arterioles of active, lesional skin are capable of dilation, increasing CBF 2-fold [11].

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